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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,202	07/29/2003	Douglas Pat Cerretti	2861-US-A	3148

7590 06/29/2005

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 06/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/633,202	CERRETTI, DOUGLAS PAT	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-29* is/are pending in the application.

4a) Of the above claim(s) *22-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-21 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20030729*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

Applicant's Preliminary Amendment filed 29 July 2003 has been entered, canceling original claims 1-12 and introducing the new claims 13-29, as well as amending the first page of the specification to state continuing data for the instant application. This amendment to the specification does not indicate the status of the parent application serial No. 09/561,779, which is now abandoned. Applicant is invited to further amend the specification to indicate the status of the parent application in response to this communication.

The disclosure is objected to because of the following informalities: Brackets flank the paragraph at page 11, lines 4-6, which is inappropriate in the text of a specification. The disclosure is also objected to because it contains embedded hyperlinks and/or other form of browser-executable code. See page 3 where there are three instances at lines 18-20. Applicant is required to delete all instances of embedded hyperlinks and/or other form of browser-executable code wherever they may occur in the specification. See MPEP § 608.01. Appropriate correction is required.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

1. Claims 13-21 and 29, drawn to an isolated polypeptide sharing at least 80% amino acid sequence identity with the region of SEQ ID NO:2 between positions 399 and 502, classified in class 530, subclass 350.
2. Claims 22-28, drawn to an isolated polynucleotide encoding a polypeptide sharing at least 80% amino acid sequence identity with the region of SEQ ID NO:2 between positions 399 and 502, to vectors and host cells comprising the polynucleotide, and to a first method of use of the polynucleotide in a method of making the encoded polypeptide, classified in class 536, subclass 23.1.

Inventions of Groups 1 and 2 are unrelated, each to the other, because each comprises a distinct product having a unique primary structure and because the protease of Group 2 is disclosed to have a different catalytic function than the polypeptide of Group 1. Inventions are unrelated if it can be shown that they are not

disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed to be used together and require separate searches in the patent and non-patent literature.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ms. Susan Lingenfelter on 10 June 2005 a provisional election was made **with** traverse to prosecute the invention of Group I, claims 13-21 and 29. Affirmation of this election must be made by applicant in replying to this Office action. Claims 22-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13-21 and 29 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility. It is agreed that SEQ ID NO:2 encodes a metalloprotease comprising a disintegrin domain and a protease domain and that both domains share detectable degrees of amino acid sequence identity with protease and disintegrin domains in the prior art. The specification, however, discloses no specific *in vitro* or *in vivo* utility for either the disintegrin domain or the protease domain of the SVPH1-26 amino acid sequence set forth in SEQ ID NO:2. The specification teaches that mRNA transcripts encoding the SVPH1-26 metalloprotease can be detected, see pages 9 and 58, in the human testis but discloses no specific or generic biological activity of the SVPH1-26 disintegrin domain identified in claim 13. The specification proposes, at page 6, the use of the SVPH1-26 disintegrin domain in assays to detect inhibitors of its undisclosed

activity and in view of the resemblance of the amino acid sequence of the human SVPH1-26 disintegrin domain with other mammalian disintegrin domains proposes, at page 9, that an inhibitor of the disintegrin domain might affect fertilization. But there is no disclosure or demonstration in the specification of any **specific** function of the SVPH1-26 disintegrin domain in mammals where the processes of spermatogenesis and fertilization occur in separate organ systems of different sexes, indicating that Applicant was unaware of the physiological role of a claimed disintegrin domain at the time the application was filed. A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). Mere allegations of a prospective, potential, utility cannot rise to the level of a credible indication of a specific utility that is substantial. Indeed, the specification's vague assertions indicate that Applicant knew no specific utility for the claimed invention at the time the application was filed that would permit the use by the public of the SVPH1-26 disintegrin domain.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-21 and 29 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 13-16, 18, 20 and 29 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 13-16, 18, 20 and 29 are rejected because they describe a polypeptide having disintegrin activity wherein a disintegrin domain may differ at as many as 20 amino acid positions, or 20% of the positions, **anywhere** within the 402-amino acid sequence of the native SVPH1-26 disintegrin domain present between amino acid positions 399 and 502, inclusive, of SEQ ID NO:2. The specification fails to exemplify or describe the preparation of the divergent amino acid sequences of variant disintegrin domains of claims 13-16, 18, 20, and 29 and neither teaches nor suggests the positions throughout the sequence of amino acids between positions 410 and 502 of SEQ ID NO:2 that might be altered or what the nature of such alterations might be. Thus the artisan reading the specification would not consider that Applicant could have predicted the structure of disintegrin domains that diverge as much as 20% from the amino acid sequence of region extending from position 399 through position 502 of SEQ ID NO:2. The specification does not otherwise disclose or suggest the nature or source of a variant disintegrin domain that meets the claim limitations. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The treatment of the claimed subject matter by the specification is entirely prospective and skilled artisans in the relevant field of molecular biology could not predict the structure of a variant disintegrin domain of claims 13-16, 18, 20, and 29.

Claims 13-16, 18, 20, and 29 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for the preparation of a disintegrin domain having disintegrin activity comprising either an amino acid sequence identical to the 104-amino acid sequence between amino acid positions 399 and 502, inclusive, of SEQ ID NO:2, or the amino acid sequence set forth in SEQ ID NO:3, does not reasonably provide enablement for amino acid sequences having disintegrin activity that diverge from the sequence of amino acids between positions 399 and 502 of SEQ ID NO:2, or the amino acid sequence set forth in SEQ ID NO:3, by amino acid

substitutions, deletions and insertions, or combinations thereof at as many as 20% of the amino acid positions of the 104-amino acid sequence between positions 399 and 502 of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification cannot support the introduction of numerous amino acid insertions, deletions, or substitutions anywhere the SVPH1-26 disintegrin domain between positions 399 and 502, inclusive, of SEQ ID NO:2 where neither the specification nor the prior art made of record, taken together, teach of suggest where so many amino acid positions in a disintegrin domain might be altered, nor teach the nature of any alterations that may be made, which permits a resulting variant amino acid sequence to function as a disintegrin domain. The specification teaches no specific disintegrin-like activity for the native SVPH1-26 disintegrin domain of SEQ ID NO:2 with which the artisan, seeking to make even a few alterations, might assay for retention of a disintegrin-like activity and mere sequence perturbation will not enable the design and preparation of divergent disintegrin domains that might provide the public domain that retains its undisclosed, native, function. It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Applying the analysis 0f enablement discussed in *Wands* to the specification's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the SVPH1-26 disintegrin domain to the extent recited in the claims,

b) the specification lacks working examples wherein the SVPH1-26 disintegrin domain is altered to the extent recited in the claims,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no members within the class of – disintegrin doamins represented by the amino acid sequence of SEQ ID NO:2

from position 399 through positions 502, inclusive, have had as many as 20 amino acid positions identified for concurrent modification.

Thus the scope of subject matters embraced by the phrases "at least 20% identity" and "at least 10% identity" is considered to be unsupported by the present specification, even when taken in combination with the teachings available in the prior art.

Conclusion

While subject to one or more rejections above under 35 U.S.C. §§ 101 and 112, claims 13-21 and 29 are free of the prior art made of record herein. Disclosures of the expressed sequence tags in EMBL Accession Nos. AA400496 and AA400588 of Hillier et al., made of record with Applicant's Information Disclosure Statement filed 29 July 2003, provide two carboxyl-terminal domains of the metalloprotease-disintegrin of SEQ ID NO:2 herein and a portion of the disintegrin domain, but neither they nor any other prior art disclosure of record, disclose an adequate fragment of a disintegrin domain of SEQ IDs NOs:2 and 3 herein that might have disintegrin activity. The closest disclosure in the record is that of Hooft van Huijsduinen, in both WO 99/07856 and **Gene**, 1998, Vol. 206, pages 273-282, both made of record with Applicant's Information Disclosure Statement, of the ADAM 16a metalloprotease comprising a disintegrin domain amino acid sequence identical to that of SEQ ID NO:2 herein, but publications were made after the October 30, 1997, filing date of Applicant's provisional application serial No. 60/063,571, wherein the claimed invention was first disclosed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is now 571.272.0933. The examiner can normally be reached between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Ponnathapura Achutamurthy, can be reached at 571.272.0928. The fax

phone number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
24 June 2005

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER